REMARKS

Applicants have amended claims 18, 21, 23, and 27 to promote clarity and also to more distinctly claim the subject matter that they regard as their invention. The amendments do not constitute new matter[1]. Applicants have also added new claims 36-46 to cover sub-groups of claim 18. Support for these new claims can be found in original claims 18-27. Note that Applicants have cancelled claims 1-17 and 28-35 directed to a non-elected invention in response to the restriction requirement mailed September 8, 2004.

Claims 18-27 and 36-46 are currently being examined. Reconsideration of the application, as amended, is respectfully requested in view of the remarks below.

Objection to the Specification

Due to a re-formatting problem, the symbol for degree Celsius ("°C") in the Specification, all occurrences, is not properly shown. See the Office Action, page 2, lines 16-17. At the Examiner's request, Applicants have rectified this error.

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 18, 21, 23, 24, and 27 on the ground that they fail to comply with the written description requirement.

According to the Examiner, Applicants have "claimed fusion proteins that encompass heat shock proteins in addition to HSP70" and have also "claimed the broad genus of fragments of polypeptides when only the species of PSA and AFP fragments are disclosed." See the Office Action, page 3, lines 14-17. Applicants respectfully address these two grounds for rejection.

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[1] The term "degenerate sequence thereof" has been added to claim 18. An amino acid can be encoded by one or more DNA triplets, i.e., degenerate codons. Therefore, the flanking regions of a polypeptide of a Hsp70 C-terminal fragment can be encoded by a number of degenerate DNA molecules. In other words, the term "degenerate sequence thereof" does not constitute new matter. The wherein clause added to claim 18, i.e., "wherein the composition is free of any human antigen that is not covalently bound," also does not constitute new matter. Support for this clause can be found in the actual example provided in the specification. See page 11, lines 26-27, i.e., "... dendritic cells were mixed with HSPs or Hsp fusion protein ... before injection." In this example, no non-covalently bound antigen was used.

First, Applicants have amended claim 18 to limit the heat shock protein and the heat shock fusion protein to those that contain a Hsp70 C-terminal fragment. A description of this fragment can be found in the Specification at page 5, lines 16-24.

As to the second ground for rejection, Applicants would like to point out that "[a] description of a genus [ ] may by achieved by means of a recitation of a representative number of [species]." See *University of California v. Eli Lilly*, 43 USPQ2d 1398 (Fed. Cir. 1997). Applicants have demonstrated that an immune response was induced by an immunogenic composition of this invention that included a fusion protein containing an antigen, PSA. See the Specification, page 15, lines 11-12. A composition containing another antigen would also induce such a response at the target site where the antigen is present. After all, as an antigen, by definition, induces an immune response, demonstrated induction of an immune response by a single antigen adequately represents operability of other antigens.

Rejection under 35 U.S.C. § 103(a)

The Examiner asserted two grounds for obviousness rejection. Applicants traverse both grounds, respectively, below.

I

The Examiner rejected claims 18-23 as being obvious over Srivastava et al., U.S. Patent 5,985,270 ("Srivastava") in view of Suzue et al., Journal of Immunology, 1996, 156:873-879 ("Suzue"). See the Office Action, page 5, lines 10-13.

The Examiner noted that Srivastava, the primary reference, teaches a composition containing "[antigen-presenting] cells, HSP70, [PSA], and a pharmaceutically acceptable carrier," but conceded that "the antigen, PSA, is **not covalently linked** to HSP70 to create a heat shock fusion protein." See the Office Action, page 5, lines 13-19; emphasis added. The Examiner further pointed out that, Suzue, the secondary reference, teaches a method of preparing a myobacteria HSP covalently linked to an antigen. See the Office Action, page 5, line 20 to page 6, line 1. Of note, the Suzue method is limited to production of **mycobacteria** HSP, not **human** HSP. See the Abstract. According to Suzue, "[t]he cellular responses to mycobacterial HSPs are profound." See the Introduction, first paragraph, lines 7-8. Human HSP, on the other

hand, is "not immunogenic per se." See Srivastava, column 2, line 28. Thus, one skilled artisan would not have equated mycobacteria HSP to human HSP.

Claim 18, the only pending independent claim, is drawn to an immunogenic composition containing a human stress protein.[2] The stress protein can be either (i) a heat shock protein ("Protein I") containing a Hsp70 C-terminal fragment, or (ii) a fusion protein ("Protein II") containing both the same fragment and a human antigen. Note that Proteins I and II share a polypeptide sequence, i.e., a specific Hsp70 C-terminal fragment recited in claim 18. Protein I and Protein II differ from each other in that the former is not associated with any antigen while the latter is covalently bound to a human antigen.

Applicants would like to point out that the patentability of an immunogenic composition containing Protein I resides in a combination of two features, i.e., presence of a specific Hsp70 C-terminal fragment and absence of an antigen. Neither Srivastava nor Suzue describes the specific Hsp70 C-terminal fragment. Further, both references teach use of an antigen.

Referring to the animal data presented in the instant Specification, a composition containing Protein I was effective in promoting survival in mice injected with tumor cells. See the Specification, page 15, lines 17-18. Specifically, 50% of the tested animals survived, compared with 0% for the untreated mice. See Table 1 of the Specification.

The patentability of an immunogenic composition containing Protein II, on the other hand, resides in a combination of one of the two above-mentioned features, i.e., presence of a specific Hsp70 C-terminal fragment, and a second feature, i.e., presence of a **human** antigen **bound covalently** to the fragment. The second feature is also not taught or suggested in the two prior art documents. Suzue teaches **mycobacteria** HSP, not **human** HSP; these two HSPs, as pointed out above, are very different in their ability to induce an immune response. As also pointed out above, the Examiner conceded that the Srivastava composition contains an antigen that is **not covalently bound** to HSP.

It was unexpectedly found that a Protein II-containing composition was even more effective in promoting survival in mice than a Protein I-containing composition, as shown in the

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[2] The term "human stress protein" covers both the heat shock protein and the heat shock fusion protein recited in claim 18, as well as functional and structural equivalents thereof. They are all encoded by a DNA sequence flanked by 5'-GCGATGCCAACGGCATCCTGAAC-3' or a degenerate sequence and 5'-CTAATCTACCTCCTCAATGGTG-3' or a degenerate sequence.

Specification at page 15, lines 17-18. Specifically, the survival rate of mice treated with a composition containing Protein II was as high as 87%, compared with 0% for the untreated mice. See Table 1 of the Specification.

For the above reasons, neither Srivastava nor Suzue suggests the two immunogenic compositions covered by claim 18, i.e., a composition containing Protein I and a composition containing Protein II. Thus, claim 18 is not rendered obvious by the two references. Neither are claims 19-23 and new claims 36-46, all of which depend directly or indirectly from claim 18.

II

The Examiner rejected claims 18 and 24-27 as being obvious over Srivastava in view of Suzue and further in view of Tong et al., Cancer Research, 2001 61:7630-7535 ("Tong").

The Examiner pointed out that Tong teaches use of systemic chemotherapy in combination with antigen-presenting cells in mouse tumor models. See the Office Action, page 7, lines 13-14. Of note, neither an antigen nor an Hsp70 C-terminal fragment is taught in Tong. Thus, Tong does not teach or suggest a composition that contains the specific Hsp70 C-terminal fragment recited in claim 18 but does not contain any antigen (i.e., a Protein I-containing composition of claim 18), or a composition that contains the same Hsp70 C-terminal fragment covalently bonded to a human antigen (i.e., a Protein II-containing composition of claim 18). Applicants therefore submit that Tong fails to cure the above-stated deficiencies of Srivastava and Suzue. In other words, claim 18, drawn to a composition containing either Protein I or Protein II, is not rendered obvious by Srivastava, Suzue or Tong. Neither are claims 24-27 and new claims 36-46, all of which depend from claim 18.

III

For the reasons set forth above, claims 18-27 and new claims 36-46 are not rendered obvious by any of the cited references. Applicants respectfully request that the Examiner allow these claims.

CONCLUSION

Based on the remarks set forth above, Applicants submit that all of the pending claims cover allowable subject matter. Early allowance by the Examiner is respectfully solicited.

Enclosed is a Petition for Three Month Extension of Time with the required fee of $510. Please apply any other charges to deposit account 06-1050, referencing attorney docket 13886-002001.

Respectfully submitted,

Date: 5-3-05

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